PNEUMONIA

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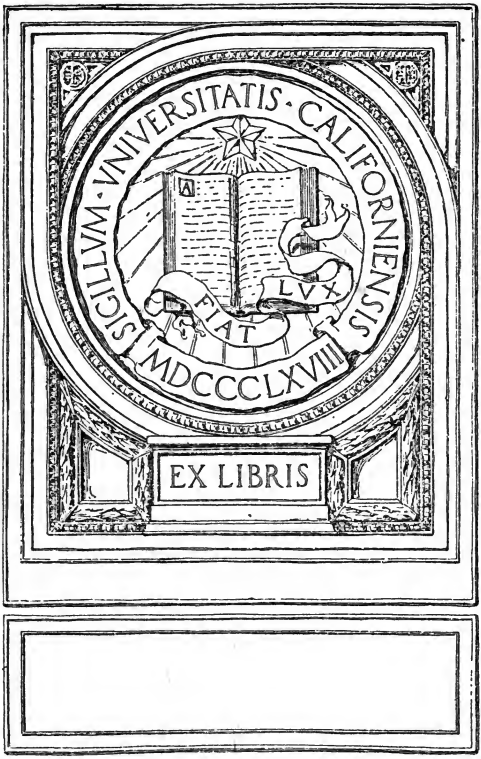
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PNEUMONIA

BY

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HARVARD HEALTH TALKS

PRESENTING the substance of some of the public lectures delivered at the Medical School of Harvard University, this series aims to provide in easily accessible form modern and authoritative information on medical subjects of general importance. The following committee, composed of members of the Faculty of Medicine, has editorial supervision of the volumes published:

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PNEUMONIA

PNEUMONIA

REFERRING to pneumonia, Osler writes: "One of the most widespread and fatal of all acute diseases, pneumonia has become the 'Captain of the men of Death' to use the phrase applied by John Bunyan to consumption."

Frequency and Importance

In this country about 10 per cent of all deaths are each year due to some form of pneumonia and this annual toll of lives has been maintained with little apparent variation for many years. Strictly comparable statistics are lacking for other communities but, making due allowance for differences in classification, a similar high prevalence seems to obtain also in other civilized countries in which mortality statistics are available.

While the disease is constantly a menace and thus termed endemic, numerous instances might be cited of more or less severe local outbreaks or epidemics at certain times and in certain places as a succession of cases in the same house, on shipboard, in hospitals and in jails. Conditions of overcrowding are largely responsible for such epidemics. In 1906 the death rate among negroes employed in the construction of the Panama Canal reached eighteen per thousand. A similar high mortality has been noted among negroes employed in the mines on the Rand and in 1912 the death rate from pneumonia was twenty-six per thousand. In Panama and on the Rand the highest mortality occurred among the recent arrivals and the mortality rapidly diminished after a short residence in the community.

We have unfortunately just passed through a period of greatly increased prevalence of pneumonia during and

after the influenza pandemic. In the absence of any reliable figures it is futile to speculate as to the number of deaths from pneumonia in the country at large during the scourge of influenza, but the importance of pneumonia as a cause of death is strikingly illustrated in the report of Vaughan and Palmer for the United States Army during the World War. Of about 4,000,000 men, about 40,000 perished in combat and 47,000 died from disease. Pneumonia accounted for more than 50 per cent of the deaths from disease prior to the influenza pandemic in 1918 and for 93.7 per cent during the period covered by the pandemic. Men from the rural districts and the southern communities suffered most severely. Excluding the influenza period from consideration, pneumonia was nine times more frequent among the men in the army than among civilians of the same age group. The high incidence of pneumonia in the army may be

ascribed to epidemics of measles and influenza followed by pneumonia, an increased opportunity for contagion in the close proximity of susceptible individuals in barracks, tents, and the mess, and a lowering of resistance from exposure, overwork, and fatigue.

Types of Pneumonia

I have thus far spoken of pneumonia without distinction as to type and before proceeding further it will be necessary to define the two recognized forms of the disease; one is spoken of as lobar pneumonia from the more or less complete involvement of one or more lobes of the lung in an inflammatory process. In this type there is practically always one group of bacteria, called pneumococci, to be found in the lung and frequently also in the blood. Lobar pneumonia is a disease with a well-defined and uniform onset, usually with initial chill, rapid elevation of tempera-

ture, pain in the side, cough and bloody expectoration, running a febrile course of about seven days and terminating abruptly in favorable cases. The second type is known as bronchopneumonia and here the bronchi or smaller air passages and even their smallest ramifications in the lungs together with the adjacent or terminal air vesicles and the neighboring lung are the site of an inflammation. In bronchopneumonia the infecting agents are usually micro-organisms normally inhabiting the mouth, and hence the bacterial flora of the mouths of normal persons to a considerable degree determines the bacteriology of the disease. The pneumococcus is the most common single cause but other organisms are also concerned and mixed infections with more than one kind of bacteria are not uncommon. In contrast to the usual, well-defined and uniform onset and abrupt termination of the symptoms in lobar pneumonia, bron-

chopneumonia presents a variable picture, occurring as a complication of conditions likely to mask or modify its manifestations and with a variable extent of lung involvement.

Causes

In considering the causes of pneumonia, it is desirable to distinguish between the predisposing and immediate causes. Among the *predisposing causes* susceptibility is increased as age advances. It is greater among males than females, probably on account of the greater opportunity for infection in occupations among males. The subjects of chronic alcoholism are somewhat more prone to have pneumonia as suggested by an apparent higher percentage of heavy drinkers in patients admitted to hospitals with pneumonia than in the other patients and in the population at large.

There is a marked seasonal variation in the incidence of pneumonia, a large

majority of the cases occurring during the months between November and June. The explanation is uncertain but the tendency to live under less satisfactory hygienic conditions in crowded and poorly ventilated rooms during cold and inclement weather may be responsible. A greater incidence of pneumonia in the city than in the country suggests that overcrowding is a factor of importance. Close contact within doors increases the opportunity for transmission of infected material from one person to another through the distribution of particles by loud talking, coughing, and sneezing in houses, theatres, halls, barracks, street cars, etc., and contamination by fingers soiled with saliva or sputum.

The increased susceptibility of recent arrivals in a community, as in the United States Army, in Panama, and on the Rand, may be ascribed to less previous exposure and consequently less acquired resistance to organisms which abound in

crowded communities. Such debilitating conditions as hunger, fatigue, exposure to wet and cold, the later stages of cardiac disease with passive congestion of the lung, malignant disease, chronic nephritis, cerebral hemorrhage and other diseases are also to be regarded as predisposing factors.

A history of acute infection such as accompanies an ordinary "cold" can be obtained in from 25 to 50 per cent of all cases of lobar pneumonia and such infections may be regarded as important predisposing factors, the specific agent of the "cold" (as yet unknown) probably acting to carry down the cause of pneumonia into the deeper parts of the respiratory tract and leading to its implantation in the lung. Measles, influenza, and whooping cough are also not infrequently followed by pneumonia, more often of the bronchopneumonic type. In these three diseases the specific cause, likewise unknown, probably acts

in similar fashion to implant the pneumococcus within the deeper parts of the tract.

Bacterial cause of pneumonia. The pneumococcus is practically the only *immediate* cause of lobar pneumonia and the most common single cause of bronchopneumonia. Our knowledge of the organism extends over a period of thirty years and goes back to its independent and almost simultaneous discovery by Sternberg in September and by Pasteur in December, 1880. Unfortunately for American medicine, Sternberg's article did not appear until April, while Pasteur's publication is dated January, 1881, and the priority of the discovery therefore belongs to Pasteur. The importance of the pneumococcus, however, was not appreciated until its frequent presence in pneumonia was established by Fraenkel in 1884 and later by Weichselbaum in 1886. It is a lance-shaped organism occurring in pairs or chains.

The pneumococcus has interesting biologic peculiarities which are doubtless concerned in its behavior as an infecting agent. It is very sensitive to change in the reaction of the media in which it grows and growth can be started in artificial media only at a reaction very close to that of the circulating blood which is slightly alkaline. In artificial media containing carbohydrate such as glucose, however, growth, once started at a slightly alkaline reaction, proceeds until the media become slightly acid, further multiplication being inhibited by the acid produced. Its extreme sensitiveness to acid may be better appreciated when it is stated that the range between the slightly alkaline reaction of normal blood and that of the culture containing glucose in which death of the organism takes place is about that between ordinary tap water and distilled water standing in the laboratory.

The lower animals vary in their sus-

ceptibility to infection with the pneumococcus, chickens and pigeons being immune, and rabbits, rats, and mice highly susceptible. The readiness with which artificial infection of these lower animals can be produced in the laboratory has led to an important addition to our knowledge of the organism and an advance in treatment of one type of the disease with consequent reduction of mortality.

The pneumococcus is found in the saliva of more than one half of all normal persons. It is only within the past ten years, however, that we have known that all types of pneumococci are not of equal importance and it will be a reassurance for me to state at once that the kind most frequently the cause of the more severe types of pneumonia is not commonly present in the normal mouth.

Types of Pneumococci

Previous to the work of Neufeld (Arb. a. d. Kais. Gesund. 1910, xxxiv, 293) in Germany and of Dochez and Gillespie (Journal Am. Med. Ass., Sept. 6, 1913, lxi, 727), in this country, it was thought that there was no essential difference in the strains of pneumococci. By the repeated inoculation of horses with different strains it has been found, however, that after a time the animal's resistance against the organisms injected is such that when its blood is taken and allowed to separate into serum and clot, the serum will protect white mice against an otherwise fatal dose of certain strains of pneumococci. The serum is not only protective but will also cure an otherwise fatal infection. It is further found that these strains against which the horse serum is effective can be recognized by a clumping or agglutination of the pneumococci when mixed in suspension with

the horse serum. By such protective and clumping experiments three so-called "fixed" types of organisms have been separated out of the great group of pneumococci. In the first column (A) of the table (page 23) the groups are indicated by the Roman numerals. The types numbered I, II, and III are the fixed types. Type IV is made up of pneumococci with apparent individual characters and resistance against one strain of this type confers no protection against other strains. It is thus spoken of as a heterogeneous group. As shown in the second column (B) Types I and II are only rarely present in the normal mouth, while Types III and IV are common. Among persons intimately associated with patients with lobar pneumonia, however, such as attendants, relatives or friends, the percentage of those who harbor Type I or II pneumococci may rise as high as 13.0 per cent. (Avery, Chickering, Cole, and Dochez. Monographs of the Rocke-

feller Institute for Medical Research, No. 7, October 16, 1917, p. 95.)

Relation of types of pneumococci to types of pneumonia. I cannot give you statistics on the incidence of the different types in bronchopneumonia but their approximate frequency is indicated by the plus signs in the column (C). As in the saliva of normal persons Type IV is most common, Type III is probably next in frequency and Types II and I are rarely present. I would like to point out also that the similar grouping in the saliva of normal persons and in bronchopneumonia is what we should expect as the infection here is usually due to bacteria commonly inhabiting the mouth and carried down into the deeper parts of the respiratory tract.

The approximate distribution of types in lobar pneumonia, determined by Cole and his associates, is shown in the fourth column (D). Out of every 100 cases about thirty are due to infection with

INCIDENCE OF TYPES OF PNEUMOCOCCI IN THE NORMAL MOUTH AND IN THE SPUTUM OF CASES OF BRONCHOPNEUMONIA AND LOBAR PNEUMONIA

	Human Beings				
A	B	C	D	E	F
Types of pneumococci	Incidence in normal mouth [1]	Incidence in broncho-pneumonia	Approximate incidence in every 100 cases of lobar pneumonia	Lobar pneumonia usual outcome approximate number of deaths in each of the preceding groups	495 cases lobar pneumonia treated with Type I serum,[2] per cent of deaths
I	0.8%	+	30	10 (33⅓%)	10.5%
II	0.0%	+	30	10 (33⅓%)	. . .
II atypical	18.2%	++	. . .	. . .	. . .
III	28.1%	+++	15	7 (50%)	. . .
IV	52.9%	++++	25	3 (12%)	. . .

[1] Avery, Chickering, Cole and Dochez, Acute Lobar Pneumonia, Prevention and Serum Treatment. Monograph of the Rockefeller Institute for Medical Research, No. 7, October 16, 1917.

[2] Cole, Nelson Loose-Leaf Medicine.

Type I, about thirty to Type II, fifteen to Type III and twenty-five to Type IV. The low incidence of Type I and II in the normal mouth and their high incidence, 60 per cent as a cause of lobar pneumonia, is in accord with the behavior of other disease-producing bacteria, such for example as the Diphtheria bacillus which may be harbored by a small proportion of normal persons without giving rise to the disease diphtheria. The limitation of Type I and II to patients with lobar pneumonia and to those in contact with such patients suggests that pneumonia due to these two types of pneumococci is largely acquired by contact with patients with or recently recovered from pneumonia, or by contact with a healthy carrier who has been exposed to a patient with pneumonia. Pneumonia due to Type I and II pneumococci is thus to be regarded as a communicable disease and such a consideration makes it desirable to isolate

patients with lobar pneumonia and thus protect other persons so far as possible. Type III and Type IV lobar pneumonias, which together represent about 40 per cent of the cases, may be regarded as due to auto-infection from organisms normally inhabiting the mouth, but increased virulence of these pneumococci or diminished resistance of the host may also be of importance in giving rise to pneumonia.

"Crisis" in Pneumonia

I have already referred to the abrupt termination of lobar pneumonia in favorable cases. This turn of events in the disease is spoken of as "crisis" and some apprehension is naturally felt by anxious relatives when this term is used, but when crisis occurs in pneumonia it is usually a favorable event, during which the temperature falls to normal without any accompanying emergency and within twelve to twenty-four hours there

is a rapid transition from a condition of great gravity to one of safety. The crisis is usually an indication of a decisive victory won by the patient against the disease.

Factors Underlying Crisis and Recovery. The determination of the factors underlying crisis and recovery from lobar pneumonia is one of the most interesting fields for research. Much valuable knowledge has already been won but there is still much to be learned. A complete explanation may be expected to open the way to still further advance in treatment. Our present conception is that recovery is a dual mechanism, on the one hand dependent on the development of a general resistance against the pneumococcus during the course of the disease and on the other certain chemical changes in the involved lung itself leading to death of the organism.

There is considerable evidence in favor of the development of a general re-

sistance (humoral immunity) during the short period from the onset to the termination of the pneumonia. The evidence is at first sight somewhat conflicting and apparently paradoxical because of the frequency with which recurrent attacks of pneumonia may occur in the same individual. This may be due, however, to the fact that the resistance acquired by one attack is sufficient to terminate that attack without affecting any lasting protection. The more recent additions to our knowledge of the different types of pneumococci suggest another and more plausible explanation. I have already referred to the increase of resistance in horses following repeated injections of different strains as a means of recognizing the fixed types of pneumococci. By such injections rabbits as well as horses can be rendered highly immune against many times the otherwise fatal dose of pneumococci of Type I, II, or III. The resistance thus artifi-

cially induced, however, is protective only against the same type of pneumococci as that used in the injection and not against any other type. While occasional instances of Type I, II, or III pneumonia in man are known to have been followed by a second attack due to the same type as that concerned in the first infection, the repetition is usually due to pneumococci of another type, suggesting that in man an immunity may be induced against one but not against another type. Other evidence is also confirmatory in man of the building up of resistance against the particular type giving rise to the pneumonia. Blood from patients with Type I, II, or III pneumonia obtained at about the time of crisis and injected into animals has the power of protecting them against an otherwise fatal dose of the same type of pneumococci. It is ineffective in protective power against any other than the same type, indicating a specific response

in the individual against the particular type giving rise to the infection but not against any other type.

Local chemical factors may also be regarded as of influence in recovery. Mention has already been made of the susceptibility of the pneumococcus to changes of reaction in the media in which it grows and of its rapid death in the presence of a slight degree of acidity. As the inflammatory process in the lung goes through its evolution two significant changes take place in the involved region. The amount of blood diminishes and the reaction, so far as we can learn from animal experiment and tests of the lung immediately after death, changes from slightly alkaline to a degree of acidity which is within the range of the acid death point of the pneumococcus. In the study of these factors we have recently found that there is an important relation between the amount of blood serum and the effect of acidity on

the pneumococcus, serum protecting the organism to a certain extent from degrees of acidity which would otherwise kill it. At an acidity corresponding to that which the inflammatory process may reach, however, the duration of life of the pneumococcus in fluid culture media without serum is only about two hours and even 100 per cent serum may not suffice to prolong the life of the culture for more than twenty-four hours. In explanation of recovery from a chemical point of view it may be conceived that as the evolution of the local process takes place with an increase of acidity and diminishing amount of serum the acid death point of the pneumococcus is reached and crisis and recovery follow.

Resolution

Another interesting aspect of lobar pneumonia is a most remarkable change which takes place in the inflammatory

process in the lung. In consequence of the infection with the pneumococcus the affected region becomes firm and solid from the presence everywhere within the smallest air spaces of great numbers of cells technically known as polymorphonuclear leucocytes or pus cells and a fine network of delicate threads which permeate the whole structure. These threads are threads of fibrin and you are all familiar with an important result of their presence in shed blood which they cause to coagulate or clot shortly after its escape from the blood vessel. At the same time or shortly after the crisis this solid lung begins to soften, sooner or later air again enters the region and finally in spite of the profound inflammatory changes through which it has passed it is restored exactly to the functional capacity existing before the pneumonia, no trace of which now remains. This extraordinary transformation is spoken of as resolution.

Factors Underlying Resolution. That resolution can occur without permanent damage to the lung itself is due to the fact that the products of the inflammatory process are poured out into the air spaces with little involvement of the framework of the lung itself in which the circulation of blood, though impaired, is still maintained. The softening of the exudate without damage to the lung tissue is accomplished by three interesting and delicately balanced factors.

The principal agent in the transformation is a peculiar substance liberated by the pus cells which have migrated to the air spaces and form part of the inflammatory process. This remarkable substance is known as an enzyme (or ferment). If you are not already familiar with the fundamental importance of enzymatic action in and outside the body, I may emphasize it by saying that to enzymatic action is to be ascribed the ripening of fruit, the tenderness and taste

of meat, the alcoholic fermentation of sugar by the yeast cell, the digestion of food in the stomach and intestines and in fact the chemical activity of all living plant or animal cells. Ferment action in the body is a powerful force for good but must be prevented from doing harm by some regulatory mechanism. Two protective factors hold it in check in the body. Enzymatic action is inhibited by the blood serum and does not take place when there is an abundance of blood. The action of enzymes is largely dependent also upon the reaction of the medium in which the enzyme occurs. Thus the enzyme of the gastric juice works best in a strongly acid medium. Two enzymes are demonstrable in the pneumonic lung, one active in slightly alkaline, neutral, and slightly acid media and another with optimum activity in still more acid media. As the evolution of the pneumonic process takes place there is an increase in cells containing ferment, a

diminution of serum containing antiferment, and a shift to an acid reaction. In the balance between cellular material and serum, enzymatic action is absent with more and present with less than about three parts serum to one part cells. Increase of cells (enzyme), diminution of serum (antienzyme), and a shift to an acid reaction thus permit of the melting away of the exudate and restoration to normal.

Diagnosis of Pneumonia

In typical cases the diagnosis of lobar pneumonia is readily made from the history of an acute onset with chill, rapid rise of temperature, pain in the side, cough with bloody expectoration and shortness of breath, and on examination the signs of consolidation in the lung. The usual occurrence of bronchopneumonia as a complication of some infection of the upper respiratory tract, the insidious onset, irregular course and

frequent absence of definite physical signs make the diagnosis of bronchopneumonia difficult and at times impossible. In fact, it often happens that the diagnosis of bronchopneumonia can only be regarded for a time as probable from the attendant circumstances, the symptoms, and the physical signs. Into the more technical aspects of the diagnosis it is not necessary for me to go.

Diagnosis of the Type of Pneumococci

The advances in treatment of one type of pneumonia by serum make it important that the diagnosis should not rest with the establishment of a pneumonia. It should be extended to determine the presence and the type of pneumococci concerned.

Favorable results of serum treatment depend on the earliest possible determination of Type I pneumococcus and it is essential that a specimen of sputum be

obtained and sent to the laboratory as soon as possible. The sputum should be from the deeper parts of the air passages. It should be collected in a small, wide-mouthed, clean and preferably sterile bottle. As the determination of type usually depends on the presence of living organisms in the sputum no antiseptic should be added to the specimen. In the laboratory a part of the specimen is examined under the microscope and a small amount injected into the abdominal cavity of a mouse. Virulent pneumococci multiply rapidly in the mouse and on removal of the abdominal fluid their type can be determined by mixing pneumococci thus obtained or small amounts of the abdominal fluid with sera obtained from horses each immunized with Type I, II, or III pneumococcus. A correspondence of the organism giving rise to the pneumonia to one of these types is indicated by a clumping or precipitation when mixed with the

corresponding serum. A diagnosis of type can thus be made usually within eight to twenty-four hours. If large amounts, two to three teaspoonfuls, of sputum can be obtained a rapid precipitation method may permit of a determination of type within a few minutes. The State Board of Health of Massachusetts determines the type without charge.

Prognosis

The outlook for life in lobar pneumonia depends upon many factors, all of which cannot be considered. In general it may be said, as shown in the table, Column E, that the total mortality is about 30 per cent. These figures represent the mortality in good general hospitals where the poorer classes are admitted. Diminished resistance from poor nutrition, overwork, fatigue, and chronic alcoholism makes the death rate somewhat higher in hospitals than may be

expected in private practice where the mortality may be 20 per cent or even less. Of the various factors influencing the outcome age is of much importance. Youth is favorable. From the sixth to the twentieth year the mortality is not far from 6 per cent. It rises steadily as age advances reaching about 26 per cent from thirty-one to forty, nearly 40 per cent from forty-one to fifty and may rise as high as 65 per cent above sixty years of age. The mortality varies also according to the type of pneumococci giving rise to the infection. As shown in this same column about one third of the cases due to Type I and Type II are fatal. Nearly one half the patients succumb to Type III pneumonia and only about one eighth to Type IV. The influence of treatment with Type I serum in lowering the mortality of Type I pneumococcus pneumonia will be considered later.

PNEUMONIA

Prevention

I want next to call your attention to certain aspects of prevention of pneumonia. This is a difficult matter and our limitations must be at once acknowledged. The high incidence of pneumonia in our army camps and the scourge of post-influenza pneumonia which swept the country in the fall of 1918 indicate that we have much to learn regarding prevention. Indeed it would almost seem from the undiminished death rate from pneumonia over long periods of years that our efforts are thus far wholly unavailing.

There are three principal means of attack upon the prevalence of the disease, one already available, the others promising for the future.

The method already available is the application to pneumonia of such knowledge as we already possess regarding the transfer of infectious material from per-

son to person in communicable disease and there is this hopeful aspect for the future, that such transfer has not been adequately avoided in the past. The more recent knowledge acquired regarding the distribution of types of pneumococci in health and disease suggests that pneumonia due to Type I and Type II pneumococci arises from direct contact with patients with pneumonia or from contact with healthy carriers who harbor these organisms in consequence of exposure to lobar pneumonia. As Type III and Type IV pneumococcus commonly inhabit the mouths of normal persons, however, the indication is less clear regarding the prevention of pneumonia due to these types. We know, however, that passage of bacteria through susceptible animals increases their virulence and transfer of pneumococci of whatever type from patients with pneumonia to those about them doubtless favors the development of

pneumonia. These considerations should be an incentive to greatly increased caution against the transfer of disease-producing pneumococci from person to person. Transfer may take place by the contact with moist sputum or utensils used by infected individuals. It may also occur by what is known as droplet infection through the inhalation of particles of moist sputum expelled by talking, coughing, or sneezing, or by the inhalation of material which through drying may contaminate the air. Medical cleanliness, in the sense of freedom from the danger of bacterial infection, must be secured in the sick room. The sputum should be expectorated into a special receptacle and this should be burned. Drying should be prevented by avoidance of long standing. Droplet infection may be avoided by placing a piece of cloth in front of the mouth during coughing or sneezing, and the cloth should be burned. Patients with pneu-

monia should be isolated to guard others against contact, droplet and dust infection. Those in attendance should wash the hands before eating in order not to carry infectious material to the mouth. The soiling of bedding or clothing should be avoided. Soiled material should be removed, handled without shaking, and sterilized. Dry sweeping or dusting of the sick room should not be permitted. Eating utensils should be kept separate and sterilized. The room vacated by a patient with pneumonia should be thoroughly cleaned and disinfected. Sunlight limits the danger of the persistence of living pneumococci in the room.

These suggestions apply to the care of the sick room. Attention must also be paid to measures to limit the spread of infectious material by the public at large. The regulations of the Board of Health forbidding expectoration in public places should be more strictly enforced. Contamination by turning the

leaves of books and public documents after moistening the finger in the mouth should be avoided.

It should be recognized that overcrowding greatly increases the danger of transfer from person to person. A factor of great importance in the army was the increased opportunity for contagion in the close contact of susceptible individuals in barracks, tents, and the mess. Such crowding is a serious menace and responsible for the loss of many lives. Though unavoidable in the face of a national emergency, the danger may be diminished by head to foot sleeping, screening by the cubicle system, and separation by screens at mess. The bedding and barracks should be thoroughly cleaned and aired. Overcrowding is to be avoided in civil as well as military life and an improvement of housing conditions in our cities will diminish contact infection. As dust is concerned in the spread of respiratory infections, the

amount of city dust and smoke should be diminished. When in any community respiratory infection reaches a menacing prevalence, mass meetings should be forbidden, schools should be closed, and infected boats should not land passengers at uninfected ports.

There are certain precautions which apply particularly to the individual. Autogenous infection with organisms harbored in the mouth is responsible for about 40 per cent of the lobar pneumonias and for a large proportion of the bronchopneumonias. Persons with an infection of the upper parts of the respiratory tract such as accompanies a "cold," influenza, tonsillitis, etc., should avoid chilling of the body, exposure to draught when insufficiently clad, and rapid cooling when overheated. The danger of inhalation of infectious material may be diminished by breathing pure air free from dust, the maintainance of an equable temperature in the house, keeping

children within doors on dusty days, the wearing of a veil out-of-doors, and careful cleaning of the teeth and mouth during the fevers and preceding any operative procedure under a general anesthetic. Operations under general anesthesia should be avoided in other than emergency cases during any nasal infection, tonsillitis, or cough, and the operation postponed until the infection has wholly subsided. In the presence of such an infection, an imperative operation should if possible be done under local rather than general anesthesia, or if general anesthesia must be used, gas-oxygen or chloroform is to be preferred to ether.

Still another matter of importance is the recognition that there is to a certain degree a predisposition to pneumonia in the lowering of resistance by an inadequate food supply, exposure, overwork and fatigue, and greater attention should therefore be paid to enough

and proper food, sufficient clothing, and a suitable balancing of activity and rest.

Preventive measures must, however, go further than this and strike more nearly at the root of the pneumonia problem and this brings us to the first of the two methods of attack with promise for the future. Such diseases as measles, whooping cough, influenza, and diphtheria in which there is an infection of the upper parts of the respiratory tract are prone to be complicated or followed by pneumonia, usually of the bronchopneumonia type. To eliminate pneumonia secondary to these diseases, the diseases themselves must be brought under control. More adequate isolation than is now customary will diminish the frequency of measles, whooping cough, and influenza, but the discovery of the causative agent and a better understanding of the mode of transmission are necessary preliminaries to complete success. It is highly important that the public

recognize our deficiencies in these matters, and recognizing them demand and financially support further investigations for the solution of the problem. Regarding diphtheria it may be said that present knowledge is sufficient entirely to stamp out the disease. The brilliant researches of the past few years have made diphtheria entirely preventable. To have it will in the future be a reproach to the intelligence or the enterprise of a community. During 1919 about 8,000 cases of diphtheria were reported in the State of Massachusetts with nearly 600 deaths. Not all persons are susceptible to diphtheria. A simple, safe, and reliable test, known as the Shick test, will determine the susceptible individuals who can then be made immune, by the injection of a diphtheria toxin-antitoxin mixture. Our State Department of Health furnishes to physicians the materials for testing susceptibility and immunization against the disease.

There is one other hopeful prospect of success in the prevention of pneumonia. Typhoid fever and small pox, once the scourge of armies, have practically disappeared as the result of preventive inoculation and it was natural to expect that the application of similar methods might diminish the incidence of pneumonia. Successful immunization against typhoid fever is accomplished by the injection under the skin of a suspension of dead typhoid bacilli. By the injection of animals with dead pneumococci of any type, a considerable degree of resistance to virulent pneumococci can be obtained. But for the production of the highest grade of resistance in animals it is necessary to inoculate the animal with living cultures.

Preventive inoculation against pneumonia by means of a pneumococcus vaccine was first attempted on a large scale by Wright among the miners in South Africa. The experience at the Premier

Mine in 1913 was promising. Among seventeen thousand inoculated the death rate from pneumonia was six per thousand while among six thousand seven hundred uninoculated the death rate was seventeen per thousand. By the use of a vaccine containing types of pneumococci prevalent in the mines, Lister later found that no cases of pneumonia of the type against which the men had been vaccinated developed during nine months of observation. Cecil and Austin at Camp Upton and Cecil and Vaughan at Camp Wheeler obtained encouraging though inconclusive results on soldiers during the World War. Cecil and Blake found that the inoculation of monkeys with dead pneumococci failed to protect them against experimental pneumonia though it lessened the mortality from the disease. For protection it was necessary to inoculate monkeys not with dead but with living pneumococci. I mention these matters to acquaint you with the problem,

which is a difficult one for the prevention of human infection and must still be regarded as in the experimental stage. Thus far there is not sufficient evidence to justify the general adoption of preventive inoculation against pneumonia.

Treatment

In discussing the treatment of pneumonia it will be most convenient to speak first of general measures and later of specific therapy.

General Measures of Treatment. Whether the patient should be treated at home or in a hospital depends largely upon the financial resources of the family. If proper medical oversight and nursing cannot be obtained at home it is better for the patient to be moved to a hospital. The decision, however, should be made early in the disease when the patient can stand the journey without undue fatigue and the transfer should be made in a stretcher with the patient lying down.

Every effort should be made to conserve the strength and resistance of the patient by rest, proper feeding, and fresh air. The elimination of toxic material may be favored by an abundance of water but too large a quantity should not be given. The patient should be absolutely at rest in bed and not allowed to sit up, moved and not allowed to move himself, fed and not permitted to feed himself. During the feeding he should remain recumbent, and liquid nourishment may be taken from a glass through a bent glass tube. There are no special indications regarding diet and the patient may take as much of simple and nutritious food as he can digest. During the early stages of the disease the diet usually consists of milk and milk preparations, broth and albumen water, with a more liberal diet as the fever subsides and the appetite returns. If the bowels have not moved a mild cathartic may be given at the outset. If abdominal

distention from gas is troublesome or if there is vomiting, all food may be stopped for a time. If necessary a daily suds enema should be given. The room should be well lighted and well ventilated and the windows thrown open to secure an abundance of fresh air. Keeping the patient out-of-doors in cold weather is unnecessary, but facilities for moving the patient into a porch adjoining the room are desirable.

Patients with pneumonia should never be left alone on account of the danger of sudden and unexpected delirium which may lead to injury or accident.

Drugs and Other Non-Specific Measures. Are there drugs or other measures of value in treatment? Various special methods of treatment have been tried at different times and in different places. Without going into the matter in detail, it may be said that with one exception the infection is beyond our control other than by such measures as tend to spare

and support the strength of the patient by careful nursing and hygiene and the alleviation of symptoms. Even by these simple means lives may be saved, more particularly in those cases in which there is a balancing between life and death, and the utmost care may turn the scale in the right directions. Special diets, drugs of various kinds, including alcohol, hydrotherapy, venesection, vaccines, etc., have not been shown to influence the course and outcome of the disease. But morphia is of great value in relieving the pain in the side which otherwise prevents sleep, aggravates the shortness of breath, and harasses and fatigues the patient. It relieves the pain, conserves the patient's strength, and may enable him better to withstand the infection. Digitalis, a drug with special action on the heart, may be of value especially in cases where there is irregularity of the heart with fibrillation of the auricles. There is promise in the course of time of the de-

velopment of a specific drug therapy. A derivative of quinine known as "optochin," discovered by Morgenroth, has been shown by experiments in animals to protect against subsequent infection and cure an otherwise fatal infection with pneumococci, but large enough doses to be effective in man are too dangerous to use and it cannot be recommended. Its discovery, however, is of great importance, as it is the first chemical agent definitely shown to have a bactericidal effect in the living body. Its discovery is a great incentive to further investigation.

Specific Serum Treatment of Pneumonia. In discussing the recognition of the different types of pneumococci, attention was called to the specific protective and curative action in animals of the serum of horses immunized against the different types of pneumococci. For the development of methods and the application of the principle of serum

therapy to human infection, we are indebted to Dr. Rufus Cole and his associates at the Hospital of the Rockefeller Institute. It has been shown that serum produced by the inoculation of horses with Type I pneumococcus is effective in the treatment of pneumonia due to Type I pneumococcus. Curative action of Type II and Type III horse serum has not been demonstrated. The evidence in favor of the use of this serum, Type I, against this particular type of infection is as follows: There is usually a striking improvement in the general condition of the patients treated with the serum, the lung involvement may cease to extend and the septicaemia is checked. A diminution of mortality is the most significant result. As shown in the table, Column E, the outlook in Type I pneumonia untreated by serum is a mortality of about one third of the cases. As shown in column F, Cole has collected a series of 495 serum treated cases of Type

I pneumonia, including 195 patients treated at the Hospital of the Rockefeller Institute, with a total mortality of 10.5 per cent, column H.

Cecil and Blake's results of serum treatment of experimental pneumonia in monkeys are a striking confirmation of the beneficial effects in man. Of five monkeys given pneumonia by intratracheal injections of otherwise fatal doses of pneumococcus Type I, all recovered following intravenous treatment with Type I antipneumococcic serum while the controls not so treated died. In this type of pneumonia in monkeys the serum exercises a specific therapeutic effect, frees the blood promptly and permanently of pneumococci, shortens the disease and greatly modifies its severity.

Serum treatment of other than Type I pneumococcus pneumonia has not proved of value and thus serum treatment is applicable to only one type of pneumonia, that due to Type I pneumo-

coccus for which Type I anti-pneumococcus serum is used. It is important that only a reliable serum be employed. In Massachusetts Type I serum is made by the State Board of Health. In New York it is supplied by the State and City Boards of Health. The serum made by the State Board of Health of Massachusetts is available without charge for citizens of the State. A question frequently asked is whether or not it is desirable to treat all cases of pneumonia with Type I serum irrespective of the type of the infecting pneumococci. This is a natural inquiry inasmuch as about one third of all cases of lobar pneumonia are due to Type I pneumococci. If the question could be answered in the affirmative and all cases irrespective of type treated with Type I serum the time necessary to make a diagnosis of the type would be saved and considerable trouble in the performance of the laboratory tests avoided. Another inquiry is whether or

not a single administration of Type I serum may not be given to the patient as soon as the diagnosis of lobar pneumonia is made and later injections only after finding that Type I pneumococcus is the cause of the process. Such a procedure would have the merit of very early administration and in the serum therapy of pneumonia as in serum therapy for diphtheria or meningitis, the earlier the treatment is begun the more successful is it likely to be. But in answer to both questions it may be said that the occurrence of certain reactions in certain individuals after the administration of alien serum make it desirable not to give serum to all patients and thus subject about two-thirds of all cases of pneumonia unnecessarily to these reactions, it being understood that in other than Type I infections the serum is ineffective. Too much stress, however, cannot be placed on the importance of the earliest possible diagnosis of the type

of organism giving rise to the infection in order that Type I infections may be treated with serum at the earliest possible moment.

Another question of interest is whether all cases of pneumonia due to Type I pneumococcus should be treated with the serum. In young children the difficulties of getting the serum into the veins are such as to make its administration undesirable.

Precautions in the Use of Alien Serum in Man. Certain precautions should always be used in the administration to man of serum obtained from an alien species such as the horse, and this applies not only to the treatment of Type I pneumonia with Type I antipneumococcus serum but also among others to the treatment of meningitis with antimeningococcus serum, the prevention and treatment of diphtheria with diphtheria antitoxic serum, and the prevention and treatment of tetanus with antitetanus

serum. All these sera are made by the immunization of horses and when the resistance of the horse is raised to a sufficient degree the horse is bled. The blood is allowed to clot and the separated serum removed and bottled ready for use. The treatment of pneumonia is by the injection of a large amount of the immune serum directly into the veins of the patient. The serum used in the prevention and treatment of diphtheria is usually injected under the skin but at times is also given directly into the veins. Antimeningococcus serum is usually given directly into the spinal canal, at times also into the veins. Antitetanus serum is injected under the skin to prevent the disease and both into the spinal canal and into the veins in treatment.

Following the administration of horse serum by any of these routes, certain symptoms of a varying degree of severity may arise in susceptible individuals. The symptoms are likely to be more

severe when large amounts of serum are injected directly into the veins and hence special caution must be exercised in this treatment of pneumonia. These symptoms have nothing to do with the preventive and curative action of the serum but arise in consequence of the entrance directly into the body of serum, containing substances of a protein nature common to the horse but foreign to human beings. Fortunately only a small proportion of patients are sensitive to horse serum and the susceptibles are easily recognized by certain simple procedures. In the first place the patient under consideration for serum treatment should always be asked whether or not he is subject to or has had hay fever or asthma, or if he has ever previously been given an injection of horse serum and an affirmative answer places him in the group of patients likely to be sensitive to serum, and indicates that special caution should be observed in the use of

horse serum. In all candidates for serum treatment, however, irrespective of the response to these questions sensitiveness to horse serum should be tested directly by what is known as an intradermal skin test performed by the injection into and not under the sterilized skin, by means of a very fine needle, of a small amount (0.02 c.c.) of sterile horse serum diluted (1:10) with normal salt solution. To prevent confusion with a local reaction due to the injection itself an equal amount of normal salt solution alone is similarly injected into another part of the skin and the two sites of injection are observed. In individuals sensitive to horse serum there develops at the site of the injection of the horse serum, usually within about five minutes a peculiar white elevation resembling nettle rash and spoken of as an urticarial wheal and surrounded by a zone of redness. The urticarial wheal slowly increases in size, may reach that of a half dollar within an

hour and then slowly subsides while the site of the injection of salt solution presents no such appearance. If the injection of horse serum is negative there is almost but not quite absolute assurance that the patient is insensitive to horse serum. As an added precaution therefore every patient to be subjected to serum treatment is first protected by a procedure which will increase his tolerance to the alien serum. This procedure is spoken of as desensitization and consists in the administration under the skin of 0.5 to 1.0 c.c. of horse serum, the absorption of which, as has been shown by animal experiment, enables even highly sensitive animals to tolerate large amounts of serum without trouble. In patients without a history of hay fever, asthma, or the previous injection of horse serum, and with negative skin tests, the intravenous administration of serum may be given within a few hours after desensitization.

Administration of Serum. The serum is usually given into a vein at the bend of the elbow. The serum should be warm and the first part of the first injection should be given slowly, fifteen minutes being occupied in giving the first fifteen cubic centimeters. The slow administration of the first fifteen cubic centimeters of serum is desirable as an added safeguard against sensitiveness to serum, the symptoms of which are likely to occur at once if they are to develop at all. With the completion of the slow injection of the first fifteen cubic centimeters, the serum may be allowed to enter the vein more rapidly, about a half hour usually being consumed in giving the first dose of 100 cubic centimeters. Subsequent doses are given usually at eight hour intervals while the temperature is 102 or above.

Stress has been laid on the precautions which should surround the administration of horse serum and if these precau-

tions are observed no unfavorable symptoms should occur in consequence of the injections. The method to be used in the administration of serum to sensitive individuals cannot be described here. For this and further details in the use of the method, Cole's article on Acute Lobar Pneumonia in Nelson's Loose-Leaf Medicine may be consulted, but before leaving the subject mention should be made of three types of reactions which may follow the intravenous use of horse serum.

Reactions following Serum Injections. During or immediately following the injection of serum in sensitive individuals there may develop what is spoken of as an anaphylactic reaction. The precautions already described are designed to avoid such reactions. When serum is given to sensitive individuals a general urticarial eruption or an asthmatic attack with rapidity and weakness of the pulse may occur. Such an attack may be

fatal. Atropine sulphate 1/120 grain and adrenaline chloride, 10 minims of a 1:1000 solution subcutaneously will usually relieve the symptoms.

A second type of reaction which may occur in consequence of serum administration is a rapid rise of temperature which usually occurs within an hour, accompanied by chill or chilliness, some shortness of breath and cyanosis and some elevation of pulse. This is called a thermal reaction. The temperature elevation is of short duration and is followed by a fall frequently to below the previous temperature level. This reaction is rather disturbing to the patient but is not dangerous.

A third consequence of serum treatment, more remote in point of time, is what is known as serum disease, which occurs in about 50 per cent of the patients, about one week or later after the last injection of serum and lasts for a number of days, or a week or more. The

symptoms are elevated temperature, urticarial skin rashes, swelling of the skin, stiff and painful joints, and enlarged glands and spleen. This condition though troublesome is not serious. A soothing skin wash and adrenaline chloride solution subcutaneously will give some relief from the troublesome itching.

Conclusions

In conclusion let me say that though pneumonia still heads the list of acute diseases most widespread and fatal to mankind and though the problem is not yet completely solved, yet much valuable knowledge has already been gained and there is a hopeful prospect of at least partial success in prevention and treatment.

Within the past ten years important advances have been made in the study of the pneumococcus. Its distribution and mode of transmission are better un-

derstood. The pneumococcus has long been known to be a common inhabitant of the normal mouth, as well as the cause of pneumonia, but it has only recently become apparent that all pneumococci are not alike in their disease producing power. The kinds most commonly the cause of the more severe types of pneumonia, Types I and II, are almost wholly confined to patients with pneumonia and to persons intimately exposed to them. This discovery, together with the knowledge that in general the passage of bacteria through animals increases their virulence, makes it desirable to regard pneumonia as a contagious disease and guard against transfer of the infectious agent from the sick to the well with much greater care than was formerly the custom. The methods of preventing such transfer are already well understood and should be much more strictly applied. Conditions of overcrowding are now known to be

important in increasing the prevalence of the disease and should whenever possible be avoided.

A most significant advance, capable of saving many lives, has already been made in the treatment of pneumonia due to Type I pneumococcus with Type I antipneumococcus serum. The earliest possible administration of the serum is essential for the best results and it is therefore imperative to make a prompt diagnosis of the type of infection.

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